United States Environmental Protection Agency

Prevention, Pesticides And Toxic Substances (7506C)

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EPA Questions & Answers

Proposed Guidance on Cumulative Risk Assessment of Pesticide Chemicals that have a Common Mechanism of Toxicity

EPA, in partnership with the U.S. Department of Agriculture, worked with the Tolerance Reassessment Advisory Committee (TRAC) to identify nine science policy issue areas that are key to the implementation of the Food Quality Protection Act (FQPA) and tolerance reassessment. In an October 29, 1998 Federal Register Notice, EPA published a framework to describe these issues and a preliminary schedule for the release of the policy and guidance documents associated with each issue area. For each policy, EPA is publishing a draft for public comment, followed by a revised document. The paper described here is one of these draft documents.

What is cumulative risk assessment and why is it necessary?

The Food Quality Protection Act (FQPA) directs EPA to consider the combined effects to human health that can result from exposure to pesticides and other substances that affect the body in similar ways. Such chemicals are said to have a common mechanism of toxicity.

A cumulative risk assessment is the process of combining exposure (the amount of a pesticide to which an individual is exposed) and hazard (the health effects a pesticide could cause) from all substances that share a common mechanism of toxicity. The risk presented by a pesticide depends on the toxicity of the pesticide and the amount of the pesticide to which a person is exposed. It is important to note that a pesticide having low toxicity but the potential for high exposure can present similar risk as a pesticide having high toxicity but very little potential for exposure. Since people can be exposed to several similar chemicals at the same time through various foods, drinking water, and from uses in and around the home, school, or recreational areas, these assessments are necessary to ensure that these exposures are considered as EPA makes decisions on pesticide uses.

How will cumulative risk assessments assist EPA's pesticide decisions?

For pesticides that act in the same way in the body (i.e., share a common mechanism of toxicity), cumulative assessments will help EPA ensure that such effects are evaluated and considered when determining if certain pesticides meet the FQPA safety standard of reasonable certainty of no harm. As a result, when considering a pesticide for registration, reregistration, or tolerance reassessment, EPA will evaluate more than just that individual pesticide's risk. The Agency will consider potential risks of those substances that affect the body in the same way.

What is EPA's proposed approach to doing cumulative risk assessment?

Assess Risks for Individual Pesticides
The risk assessment process begins with publication of the preliminary risk assessment on an individual pesticide. The individual chemical risk assessment is provided to the public for comment according to EPA's process for involving the public in risk assessment and risk management decisions.

As part of an individual chemical risk assessment, EPA also performs an aggregate risk assessment (considering all combined sources of exposure) for each chemical. In the aggregate assessment, EPA considers exposures to the pesticide from food, drinking water, and residential/non-occupational sources. At this stage, if risks exceed EPA's level of concern, the Agency would take steps to reduce risks associated with the chemical to acceptable levels. EPA published draft guidance on aggregate risk assessment ("Guidance for Performing Aggregate Exposure and Risk Assessments") for public comment November 10, 1999 (64 FR 61343).

Identify Pesticides with a Common Mechanism
Following the individual risk assessment, EPA identifies chemicals that have a common mechanism of toxicity, which is called a "common mechanism group." Such a group consists of chemicals for which scientifically reliable data demonstrate that the same toxic effect occurs in or at the same organ or tissue by essentially the same sequence of major biochemical events. EPA guidance on the process for identifying whether chemicals have a common mechanism ("Guidance for Identifying Pesticide Chemicals and Other Substances that Have a Common Mechanism of Toxicity") was issued on February 5, 1999 (64 FR 5795).

Perform a Cumulative Assessment
After establishing the common mechanism group, EPA will perform the cumulative risk assessment in four steps:

1. ***Hazard Assessment and Characterization***–This step identifies the potential health effects that can be caused by a pesticide. For the cumulative assessment, this includes the potential for health effects from exposure to multiple chemicals with a common mechanism of toxicity, including consideration of conditions that will allow the effects to cumulate and whether specific subgroups might have increased sensitivity to the common toxic effect.

2. ***Dose-Response Assessment and Characterization***–This step determines the health effects that occur at different levels of exposure (or doses). The cumulative assessment will consider how multiple chemicals interact with respect to different doses.

3. ***Exposure Assessment and Characterization***–This step assesses how much of the pesticide people are exposed to through food, drinking water, and various non-agricultural uses, such as use in and around the home. For the cumulative assessment, EPA will assess the potential for

humans to be exposed to multiple members of the common mechanism group and whether there are regional or subpopulation concerns.

4. ***Risk Characterization***–This step identifies the risk of health effects that could result from exposure to the pesticides, the major chemical contributors to the cumulative risk, and any subpopulations that are at increased risk.

The first two steps include use of a weight-of-the-evidence approach to determine the harmful effect that occurs through a common mechanism of toxicity and to establish a common measure of toxic potency. A weight-of-the-evidence approach involves reviewing all pertinent data and information, assessing the strengths and weaknesses of the data, and reaching conclusions based on the overall picture provided by the data, rather than based on any one specific study. One way of comparing toxic potency is by selecting one chemical as the "index" chemical (generally the one for which the Agency has the best information on effects at a variety of doses) and comparing the other chemicals to it to determine their relative potency (e.g., one might be half as toxic as the index chemical, while another might be twice as toxic).

Steps 3 and 4 include estimating exposure and risks for the food, drinking water, and residential/non-occupational pathways. Ideally, these exposures would be added. However, the data currently available for drinking water and residential/non-occupational exposures are less complete in many cases than data on exposures in food. There are several possible ways to address this problem, including the use of surrogate, or bridging, data for pesticides with similar use patterns to estimate residential exposures more realistically.

How is EPA addressing combined pesticide exposures?

The ideal data for assessing cumulative exposure should reflect realistic exposures, be taken close to the exposed individual, represent geographic, demographic, and temporal variability, and reflect actual co-occurrence of pesticides. When data for one or more of the pathways (food, drinking water, and non-occupational exposure) do not allow for a comparable level of analysis, EPA's cumulative assessment will describe the risks related to each pathway but may not combine them.

EPA's analysis would provide information on a national or regional level for food exposures, on a regional or multi-state level for non-occupational exposures, and on a local level for drinking water exposures. Thus a cumulative assessment is not a single numerical result, but is a set of geographically distributed assessments, showing the variability in risk in different areas, which would inform regulatory decisions.

The Agency is making a concerted effort to develop or obtain new data and more sophisticated exposure and risk assessment methods. The following are examples of projects underway to gather new data.

- EPA's Office of Research and Development is planning and conducting studies concerning exposures to infants and children through pathways other than food.

- EPA has called in data from registrants for several non-dietary routes of exposure including dermal contact and hand/object-to-mouth contact with contaminated surfaces and toys.

- Registrants are conducting studies on their own initiative that are generating exposure data for food, drinking water, and residential/non-occupational sources.

- EPA is developing and proposing through its science policies better methods for assessing exposure and risk, and is seeking ideas, feedback, and recommendations from the Scientific Advisory Panel and the public.

How and when will EPA apply uncertainty factors in the cumulative risk assessment process?

A composite, group uncertainty factor will be applied after estimating cumulative risk. This uncertainty factor will account for differences among individuals within a species and between test animals and humans, as well as uncertainties that are common and inherent to the chemical group. EPA also is proposing to review the scientific information to determine application of an appropriate FQPA safety factor for the group.

What are the next steps for this guidance document?

The comment period on this document closes August 28, 2000. EPA will then review the comments, solicit scientific peer review, and revise the draft document as appropriate.

How can I get more information?

The draft document, as well as other science policy documents undergoing public review, is available electronically on EPA's web site at http://www.epa.gov/trac/science/. It is available via fax-on-demand by using a faxphone to call 202-401-0527 and selecting item 6049. It also is available from the OPP docket. Call 703-305-5805 for information.